REMARKS/ARGUMENTS

(1)

The Examiner makes the restriction requirement final, and restricts continued prosecution to claims 109-144, with the species of Compound 30. Applicants cancel claims 1-108 and reserve the right pursuant to 35 U.S.C. § 121 to file one or more divisional applications directed to the non-elected subject matter during the pendency of the present application.

(2)

The Examiner rejects claims 109, 111, 112, 117, 119, 121, 122-124, 129, 131, 133-136, 141 and 143 under 35 U.S.C. § 112, Second Paragraph on the ground that the rejected claims are allegedly indefinite. Specifically, the Examiner alleges that the claims employed the language "comprising" in defining different Markush members of the compounds or moieties. The Examiner recommends the term "consisting of".

Applicants amend claims 109-112, 119, 121-124, 131, 133-136, and 143 in accordance with the Examiner's recommendation; no new matter is added by the amendment. The Examiner is respectfully requested to withdraw the pending rejection in view of the amendment. Claims 117, 129, and 141-142 are cancelled, which obviates the rejection of these claims.

(3)

The Examiner rejects claim 109, 112, 121, 124, 133 and 136 under 35 U.S.C. § 112, Second Paragraph alleging the claims are indefinite in regards to M, R_{14} and "E or Z".

a) With regard to M

The Examiner alleges that the scope of "M" is not ascertained. The Examiner says "'M' is part of a compound which is structural for the compounds. There is no nexus of the functional limitation, i.e., 'capable of complexing with a deacetylase catalytic site' as claimed. It is unclear what constitutes such functional moiety." The Examiner recommends that the structure of the moiety be clearly identified.

Applicants amend independent claims 109 and 121 to specify that M is selected from the

group recited in original claim 117; claim 117 is thus canceled. No new matter is added by the amendment. Applicants believe the amendment overcomes the Examiner's rejection and respectfully request the withdrawal of this rejection.

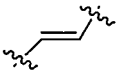
b) "substituent that is convertible *in vivo* to hydrogen"

The Examiner rejects claims 112 and 136 on the basis that the recitation "R_{14} comprises a member selected from the group consisting of hydrogen and *a substituent that is convertible in vivo to hydrogen*" renders the scope of the claims unclear because "claims 112 or 136 actually broadened the scope of the Markush members of R14 in the base claims."

Applicants understand this to be a rejection for allegedly improper dependency of claims 112 and 136. Applicants bring to the Examiner's attention that the same dependency issue applies to claim 124. Applicants amend the definition of R_{14} in claims 109, 121 and 133 to include "a substituent that is convertible *in vivo* into hydrogen." As a result of the amendment, claims 112, 124 and 136 properly depend from claims 109, 121 and 133, respectively. Accordingly, this rejection may be withdrawn.

c) E and Z

The Examiner rejects claim 133, alleging that the meaning of "L is E, Z or mixtures of E/Z -CH_2=CH_2-" is unclear because no definition of E or Z was defined and Z has been defined always to be part of a ZQ group.

Applicants submit the terms "E" (entgegen) and "Z" (zusammen) are commonly used and well known descriptors for the relative orientation of substituents on a carbon-carbon double bond; the terms 'E, Z, and mixtures of E/Z' would have been understood by persons of ordinary skill to refer to the stereochemistry about the double bond of the linker L. In claim 133, E, Z, and E/Z describe the isomeric state of the ethenylene group: E ethenylene is  , Z-ethenylene is  , and mixtures of E/Z refers to a mixture of the two isomers.

Applicants appreciate the Examiner pointing out an error in the structure delineated in the claims, which is inconsistent with the scientific base of chemistry. The structure "-CH_2=CH_2-" appears to show two pentavalent carbons. Applicants amend claim 113 to correct this error and

also add clarifying language for "E" and "Z". Amended claim 113 recites "L is selected from the group consisting of the (E) isomer of -CH=CH-, the (Z) isomer of -CH=CH-, and a mixture of (E) and (Z) isomers of -CH=CH-." The person of ordinary skill would have known that the pentavalent carbons were a drawing error. Moreover, in view of the description of the linker is having a double bond as 'E, Z or a mixture of E/Z,' the person of ordinary skill would have realized that the structure for L should have been –CH=CH- instead of $-CH_2=CH_2-$. That makes the structure of L consistent with the stereochemical designations provided in the claim. Both the error in the way L was drawn (having pentavalent carbon atoms) and the correction (removal of the subscripts '2' so the carbon atoms of linker L are tetravalent, as they must be, and so they also form a double bond, which makes them consistent with the use of the E and Z isomer designations) would have been obvious to a person of ordinary skill; therefore, the correction of that error is not new matter. In re Oda, 443 F.2d 1200, 1206 (CCPA 1971).

Further, Applicants amend claims 121 and 133 to remove the reference to Z, thereby eliminates any confusion with the (Z) descriptor of the isomers.

Applicants believe the usage of the terms (E) and (Z) in amended claim 133 is clear and was inherently disclosed in the original claim, and respectfully request the Examiner to withdraw this rejection.

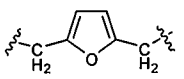
(4)

The Examiner rejects claims 109 and 121 under 35 U.S.C. § 112, First Paragraph, allegedly for failing to comply with the enablement requirement. The Examiner alleges "the scope of 'L is a substituent providing between 2-10 atoms' encompassed any atoms of the periodic table. No starting material for such compounds wherein L is 2-10 any atom other than 'C' can be found. Especially, such material such as peroxides, disulfides etc. are extremely unstable to have pharmaceutical utility. Absent of starting material, the specification offered mere language rather than enablement."

Applicants respectfully submit that the Specification as filed provided enablement for groups having non-carbon atoms as well as L groups having only carbon atoms. The MPEP §2164.01 sets forth the test of enablement as "whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in

the art without undue experimentation". United States v. Telectronic, Inc., 857 F. 2d 778, 785 (Fed. Cir. 1988). However, "a patent need not teach, and preferably omits, what is well known in the art." In re Buchner, 929 F. 2d 660, 661 (Fed. Cir. 1991); Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384 (Fed. Cir. 1991). Applicants submit that the current disclosure when filed, contained sufficient information when combined with information known in the art, to enable those skilled in the art to make and use the claimed invention where the L groups contain atoms other than carbon.

Applicants submit the disclosure taught that the L group was incorporated into the molecule as an aldehyde derivative of -Q-L-acyl via a cyclization reaction that forms the imidazole ring from a diamine plus a benzaldehyde. See, Scheme 1, page 98, coupling of Compounds 2 and 3 to form Compound 4. With a suitable benzaldehyde containing a group that corresponds to L having atoms other than carbon, those skilled in the art would know how to prepare the compounds of the invention by following the synthesis scheme disclosed, including those where the atoms of group L are not all carbon atoms.

Applicants further submit that benzaldehydes having L groups in which the atoms providing the 2-10 atoms separation between Q and M are not all carbon atoms were well known in the art when the application was filed. For example, Beilstein reports preparations of (3-formyl-phenoxy)-acetic acid derivatives at least as early as 1886 (see Exhibit A, where L = $-O-CH_2-$). It also reports availability of (5-formyl-2-hydroxy-3-methoxy-benzylsulfanyl)-acetic acid at least as early as 1993 (see Exhibit B, where L = $-CH_2SCH_2-$). It also reports availability of 4-[2-acetylamino-3-(3-formyl-4-phosphonooxy-phenyl)-propionylamino]-4-dipentylcarbamoyl-butyric acid at least as early as 1998 (see Exhibit C, where L = $-(CH_2)_3-N-(CH_2)_3-$). Further, benzaldehydes where the L moiety includes a heterocyclic group in the chain were also known in the art. For example, Beilstein reports preparation of [5-(3-formyl-benzyl)-furan-2-yl]-acetic acid methyl ester at least as early as 1997 (see Exhibit D where L = ). Thus, starting materials to enable preparation of compounds with L groups having oxygen, sulfur and nitrogen atoms and heterocycles within the chains were available in the art before the application was filed. As stated in the MPEP, the enablement analysis includes consideration of knowledge in the prior art; thus the availability of these starting materials,

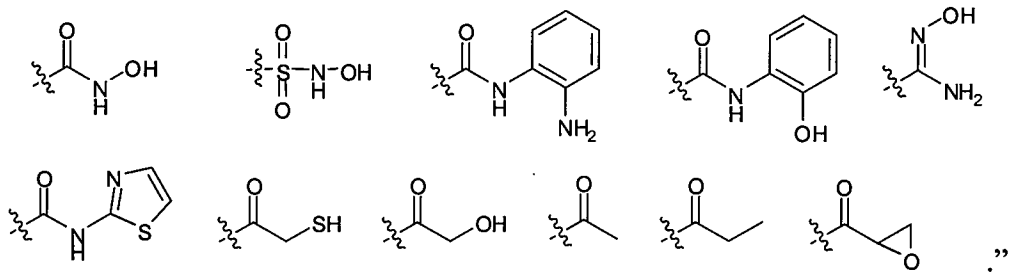
combined with the methods taught in the specification would have enabled a person of ordinary skill to prepare compounds across the scope of the invention. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection of claims 109 and 121 under 35 U.S.C. § 112, First Paragraph.

In addition, Applicants add new claims 174 and 175 which depend from claims 109 and 121, respectively, and particularly recites that the backbone atoms of the L group are all carbon atoms. No new matter is added by the amendment, and the new claims are not susceptible to this rejection because it contains no linking atoms other than carbon.

(5)

The Examiner rejects claims 109-112, 115, 121-124 under 35 U.S.C. §103(a) as being unpatentable over Vourloumis et al. Tetrahedron Lett. ("Vourloumis") in view of CA139:133505. The Examiner alleges that prima facie obviousness is established because: a) compounds similar to the benzimidazole-piperidine, i.e., the elected compounds were synthesized (Figure 1, p. 2807 and formula 8, p. 2808 which has been delineated as RN569355-84-6 in CA); b) the compounds of Vourloumis et al. and those of the instant claims are positional isomers (1-(4-piperidinyl)-benzimidazoles vs. 1-(3-piperidinyl)-benzimidazoles), and Vourloumis suggested that variation of the exemplified compounds is expected to have similar biological activity, i.e., benzimidazole scaffold is the basis for activity; and c) position isomerism has long been guided by the courts to be prima facie structural obvious.

Applicants submit that Vourloumis does not make obvious the current invention because Vourloumis in view of CA139:133505 do not teach all the elements of the independent claims. Amended independent claims 109 and 121 recite that "M is selected from a group consisting of trifluoroacetyl (-C(O)-CF_3), -NH-P(O)OH-CH_3, sulfonamides (-SO_2NH_2), hydroxysulfonamides (-SO_2NHOH), thiols(-SH), and carbonyl groups having the formula -C(O)-R_{13} wherein R_{13} is hydroxylamino, hydroxyl, amino, alkylamino, and an alkoxy group." Independent claim 133 recites that "M is selected from the group consisting of



."

As alleged by the Examiner, Vourloumis teaches only compounds wherein M is a nitro group (See, Vourloumis, p. 2802, Scheme 1, step d starting compounds 7a to 7e). CA139:133505 teaches only compounds where M is nitro or chloro (See, CA139:133505, Library I, where R_2 is 3-$O_2NC_6H_4$, 3-pyridyl, and 2-O_2N-3-ClC_6H_3). Vourloumis in view of CA139:133505 therefore do not teach or suggest an M group within the scope of the claims; accordingly, they do not render obvious the compounds of the present invention. Applicants respectfully request withdrawal of the rejection of claims 109 and 121 and the claims depending therefrom under 35 U.S.C. § 103(a).

(6)

The Examiner provisionally rejects claims 109-144 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the pending claims of copending Application No. 10/803,575. The Examiner alleges that even though the conflicting claims are not identical, they are nevertheless not patentably distinct because the instant claims are fully embraced by the copending scope. The Examiner suggests that a timely filed terminal disclaimer may be used to overcome the rejection.

Applicants note that the conflicting application No.10/803,575 is commonly owned with the current application. Applicants request that this rejection be held in abeyance until allowable and overlapping subject matters have been identified.

(7)

Applicants further amend claims 110-116, 118-120, 122-128, 130-132, 134-140 and 143-144 to correct informalities; no new matter is introduced by the amendments.

(8)

Applicants added new claims 145-154 which depend from claim 109 and claim selected M substituents recited in claim 118 independently; no new matter is added by the amendment.

(9)

Applicants added new claims 155-164 which depend from claim 121 and claim selected M substituents recited in claim 130 independently; no new matter is added by the amendment.

(10)

Applicants added new claims 165-173 which depend from claim 133 and claim selected M substituents recited in claim 130 independently; no new matter is added by the amendment.

(11)

Applicants add new claims 174 and 175 which depend from claims 109 and 121, respectively, and particularly recite that the backbone atoms of the L group are all carbon atoms. No new matter is added by the amendment.

(12)

Applicants add new claims 176 and 177, and amend claim 144 to claim a particular -L-M group. Support for the amendment may be found in original claim 133; no new matter is added by the amendment.

CONCLUSION

Applicants earnestly believe that they are entitled to letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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